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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/981,286 | 10/15/2001 | Stanley J. Watowich | 265.00260101 | 4993 |

7590 07/28/2004

Attention: David L. Provence
Mueting, Raasch, & Gebhardt, P.A.
P.O. Box 581415
Minneapolis, MN 55458-1415

| EXAMINER | |
|---|---|
| ZHOU, SHUBO | |
| **ART UNIT** | **PAPER NUMBER** |
| 1631 | |

DATE MAILED: 07/28/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/981,286 | WATOWICH ET AL. | |
| | Examiner | Art Unit | |
| | Shubo (Joe) Zhou | 1631 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *22 September 2003 and 30 April 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-34* is/are pending in the application.

4a) Of the above claim(s) *1-24 and 30-34* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *25-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *22 September 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

1. Applicants' amendment and request for reconsideration in the communication filed on 4/30/04 and 9/22/03, is acknowledged and the amendments entered.

2. Applicant's arguments in response to the previous Office action have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous Office actions are hereby withdrawn. The following rejections and/or objections are reiterated from the previous Office action, mailed 5/20/03, and constitute the complete set presently being applied to the instant application.

3. This application contains claims 1-24, and 30-34 drawn to an invention nonelected with traverse in the communication filed 3/26/03. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

### *Information Disclosure Statement*

4. The citations/listings of publications and/or patents in various sections of the specification such as those on page 10, etc. are not a proper Information Disclosure Statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

### *Specification*

5. The specification is objected to because of the following:

6. It is noted that trademarks are used in this application, such as GENBANK™ (registered by United States Department of Health and Human Services) on page 2 and elsewhere (added by the amendment filed 4/30/04). Trademarks should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner that might adversely affect their validity as trademarks.

7. Appropriate correction is required.

8. The amendment to the specification filed 4/30/04 is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows:

The amendments to the specification at page 2 and elsewhere added GENBANK™ accession number L01443 in place of the original SEQ ID NO:1. This is considered as new matter because a database entry with accession number is subject to modification and thus the sequence therein is subject to alteration, unlike the sequence of SEQ ID NO:1 in the application which is set forth in the Sequence Listing.

Applicant is required to cancel the new matter in the reply to this Office Action.

***Claim Rejections-35 USC § 112***

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 25-29 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

In *In re Wands* (8 USPQ2d 1400 (CAFC 1988)), the CAFC considered the issue of enablement in molecular biology. The CAFC summarized eight factors to be considered in a determination of "undue experimentation". These factors include: (a) the quantity of experimentation; (b) the amount of guidance presented; (c) the presence or absence of working examples; (d) the nature of the invention; (e) the state of the prior art; (f) the predictability of the art; (g) the breadth of the claims; and (h) the relative skill in the art. The factors are analyzed for the instant case as follows:

(a) In the instant case, the amount of experimentation required by a skilled artisan in order to practice using the claimed method to identify a polypeptide that prevents cell death after exposure of the cell to a pathogen or toxin would require an unpredictable amount of experimentation for the following reasons:

(b) There is no guidance in the instant specification that teaches the skilled artisan how to use the claimed methods to identify a polypeptide comprising a fragment of VEE capsid protein

that prevents cell death after exposure of the cell to a pathogen or toxin. While the specification indeed provides guidance to making a collections of polypeptides comprising a fragment of the VEE capsid protein and introduce them into cells, it fails to provide sufficient guidance with respect to the structures, especially conformations, and properties of the polypeptides, neither does it provide guidance as to the structures and components of pathogens or toxins, as well as their potential interactions with the collection of polypeptides, which are all critical factors for successfully identifying a polypeptide comprising a fragment of VEE capsid protein that prevents cell death after exposure of the cell to a pathogen or toxin.

(c) The instant application does not present any working examples wherein the claimed methods are used to have actually identified a polypeptide from a collection of polypeptides comprising a fragment of VEE capsid protein that prevents cell death after exposure of the cell to a pathogen or toxin.

(d) The nature of the invention, a method for identifying a polypeptide from a collection of polypeptides comprising a fragment of VEE capsid protein that prevents cell death after exposure of the cell to any pathogen or any toxin, is complex, especially given the extreme diversity of pathogens and toxins and the high complexity of the structures and properties thereof. For example, a pathogen can be a multi-cellular organism, a unicellular bacteria, a virus, or any substance that causes a disease (Stedman's Online Medical Dictionary, 27th Edition, **pathogen:** Any virus, microorganism, or other substance causing disease), and a toxin may have any chemical structure and exert its effect in any may or form (Stedman's Online Medical Dictionary, 27th Edition, **toxin:** A noxious or poisonous substance that is formed or elaborated either as an integral part of the cell or tissue, as an extracellular product (exotoxin), or as a

combination of the two, during the metabolism and growth of certain microorganisms and some higher plant and animal species).

(e) The prior art does not teach or suggest the claimed invention: displaying a collection of fusion polypeptides of a fragment of VEE capsid protein with other random polypeptides in vivo, exposing a cell comprising such fusion polypeptides to pathogens or toxins, and identifying a polypeptide from the collection that prevents the death of the cell. The prior art does teach displaying certain fusion polypeptides in vivo and identifying polypeptide that disturbs a particular cellular pathway. For example, Caponigro et al. (Proc. Natl. Acad. Sci. USA, Vol. 95, pages 7508-7513, June 1998) teach using the green fluorescent protein (GFP) as a scaffold to display peptides *in vivo* and screening for peptide that inhibits the pheromone response pathway in yeast. See the entire document, especially pages 7508-7511. Norman et al. (Science, Vol. 285, pages 591-595, July 1999) teach using a highly expressed and biologically inert carrier protein derived from staphylococcal nuclease to display random peptides in vivo and selecting peptide that inhibits the pheromone signaling pathway, transcriptional silencing and the spindle checkpoint. Further, Norman et al. stress the importance of maximum expression of the random polypeptides in vivo (see page 591) and the requirement of a reliable test for verifying the potential candidates because of the very high rate of false positives and false negatives. See page 594.

(f) The prior art does not address predictability with regard to a successful identification of a polypeptide from a collection of polypeptides displayed in vivo that inhibits cell death after exposure of the cell to a pathogen or toxin. In general, the prior art does not address the predictability of identifying a polypeptide that inhibits a particular biological or cellular pathway.

(g) The claim to a method of identifying a polypeptide from a collection of polypeptides comprising a fragment of VEE capsid protein that inhibits cell death after exposure of the cell to a pathogen or toxin in claim 25 is broad because it can be any polypeptide comprising a fragment of VEE capsid protein as required in the claim and it can be any pathogen or any toxin, which possesses broad range of structures and properties. Even for the dependent claims 26-29, they are also broad in that there is a great amount of different viruses or microbe (claim 26), bacterium, rickettsia or fungus (claim 27), biological toxins (claim 28) or chemical toxins (claim 29).

(h) The level of skill of those in the art who practice identifying a polypeptide from a collection of polypeptides displayed in vivo that inhibits a particular biological or biochemical pathway is high.

The skilled practitioner would first turn to the instant specification for guidance in practicing a method to identify a polypeptide from a collection of polypeptides comprising a fragment of VEE capsid protein displayed in vivo, that inhibits cell death after exposure of the cell to a pathogen or toxin, as claimed. However, the specification does not provide sufficient guidance for successfully practicing the method as claimed to achieve its objective, i.e. obtaining a polypeptide comprising a fragment of the VEE capsid protein that inhibits cell death in response to a pathogen or toxin. As such, the skilled practitioner would turn to the prior art for such guidance. However, the prior art does not teach or suggest the means to practice a method for identify a polypeptide from a collection of polypeptides comprising a fragment of VEE capsid protein displayed in vivo, that inhibits cell death after exposure of the cell to a pathogen or toxin, as claimed. Finally, said practitioner would have to turn to trial and error experimentation to identify a polypeptide comprising a fragment of the VEE capsid protein that

inhibits cell death in response to a pathogen or toxin, without guidance from the specification or the prior art. Therefore, undue experimentation becomes the burden of the practitioner.

11. Applicant's arguments filed 9/22/03 have been fully considered but they are not persuasive for the following reasons:

Applicants first argue that the specification provide guidance to making the polypeptides containing a fragment of the VEE capsid protein, that the specification provides a prophetic example, and that description of the structures of the polypeptides and pathogens and toxins are not required for enablement because the references cited by the Office, Caponigro et al. and Norman et al. did not do so. See pages 19-22 of applicants' response. This is not persuasive because firstly providing guidance to making a polypeptide is not equivalent to providing guidance to identifying a polypeptide comprising a VEE capsid protein frament that inhibit cell death caused by a pathogen or toxin. Secondly, the inventions of Caponigro et al. and Norman et al. are not the same as the claimed inventions of the instant application. The examiner cited the references to show that the claimed invention is not taught in the prior art. The experimental settings in the references, compounds to screen, etc. are all different from the claimed invention. Further, the references do provide working examples not prophetic examples.

Applicants then argue that some experimentation is permissible if it is routine for enablement, and that practicing the claimed invention does not require undue experimentation. See pages 23-24. This is not deemed persuasive because as analyzed above, and as set forth by the court (*In re Wands* (8 USPQ2d 1400 (CAFC 1988)), all the factors from (a) to (h) are analyzed as a whole to determine whether undue experimentation is required for practice the

claimed invention. All factors considered, especially given that no working example is provided; no guidance to identifying the polypeptide for inhibiting cell death against pathogen or toxin; the prior art does not teach the invention, and the complex nature and the extremely broad scope of the claims, a killed artisan would have to turn to trial and error experimentation to identify a polypeptide comprising a fragment of the VEE capsid protein that inhibits cell death in response to any pathogen or toxin. Therefore, undue experimentation becomes the burden of the practitioner.

***Conclusion***

12. No claim is allowed.

13. **THIS ACTION IS MADE FINAL.**

14. Applicants are reminded of the extension of time policy as set forth in 37 C.F.R. §1.136 (a). A shortened statutory period for response to this final action is set to expire three months from the date of this action. In the event a first response is filed within two months of the mailing date of this final action and the advisory action is not mailed until after the end of the three-month shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R. §1.136 (a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than six months from the mailing date of this final action.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shubo (Joe) Zhou, whose telephone number is 571-272-0724.

The examiner can normally be reached Monday-Friday from 8 A.M. to 4 P.M. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, Ph.D., can be reached on 571-272-0722. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to Patent Analyst Tina Plunkett whose phone number is (571) 272-0549.

16. Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public. For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Shubo (Joe) Zhou, Ph.D.

Patent Examiner

23 July 2004

JOHN S. BRUSCA, PH.D
PRIMARY EXAMINER